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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,515	11/28/2001	Shuqian Jing	00-659-A	1848

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EXAMINER	
ANDRES, JANET L	

ART UNIT	PAPER NUMBER
1646	4

DATE MAILED: 06/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,515	JING, SHUQIAN	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears n the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *9,12-42,46-49 and 51-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11,43-45,50,56 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 10 is acknowledged. Claims 1-57 are pending in this application. Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are under consideration in this office action. Claims 9, 12-42, 46-49, and 51-55 are withdrawn from consideration as being drawn to a non-elected invention.

Specification

2. The use of the trademarks QIAGEN (pp.33, 43, 86), READY-TO-GO (p. 79), PERCOLL (p. 83), and SUPERSCRIPT (p. 86) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

3. Claim 50 is objected to as depending from non-elected claims.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are drawn to a polynucleotide encoding a TGF-β-related protein and methods of expressing same. The claimed polynucleotide is not supported by either a specific and substantial asserted utility or a well-established utility.

A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" use for the claimed invention. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966):

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

The specification fails to provide objective evidence of any activity for the encoded protein or to show that this protein even exists. Further, while applicant lists a number of diseases in which the encoded protein might be involved (pp. 75 and 76), the specification does not disclose any diseases or conditions known to be associated with the encoded protein. Merely listing a number of possibilities is not sufficient to identify or confirm a "real world" context of use; clearly further research would be required to identify a disease in which the encoded protein is involved. Thus the use of transgenic animals to screen drugs, described on p. 54, is not a substantial utility; further research is required to identify a purpose for such screens. Similarly, there is no specific and substantial utility associated with screens for modulators of TGF-β-R, as described on pp. 54-58, since one of skill would not know what activity would be expected to be modulated by a molecule so identified. There is no "real world" use associated with the study of modulators of a protein whose significance itself is unknown. This is a research use with the intended goal of discovering how the protein might be used or what use might be associated with

the ability to affect it, not a use for the protein itself. Cell-specific expression, set forth on p. 59, is not specific to the claimed polynucleotides, nor does the specification teach any particular specificity or provide information as to how the polynucleotides could be used to identify cell lineage.

Thus, further research is required to identify a disease for which TGF-β-R could be used, or a disease for which its presence would be diagnostic. See Brenner v. Manson, noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment.

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The specification identifies TGF-β-R as a member of the TGF-β family and teaches on p. 75 that it is most closely homologous with GDF-3. Identifying a polynucleotide as encoding a protein of this family does not endow the polynucleotide with a specific and substantial utility. Proteins of this family are known to function in many different physiological contexts: Miyazano et al. (J. Cell Physiol. 2001, vol. 187, pp. 2655-276) teaches that there are more than 30 members of this family (p. 266, column 2) and that they are involved in many different processes (p. 266, column 2, - p. 267, column 2; figure 2, p. 271). No receptor or function is identified for GDF-3 by Miyazano et al. and the instant specification provides no compensatory guidance as to what function might be associated with a limited homology to this protein. There is therefore no well-established utility associated with identification of TGF-β-R as a member of the TGF-β family; they are involved in many different processes and utility is specific to the individual protein.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, were it enabling for a polynucleotide comprising SEQ ID NO: 1 or 3, would still not reasonably provide enablement for variants and fragments of the polynucleotide. Since the biological activity of the parent polynucleotide is not defined in the specification, one of skill in the art would not be able to make nucleic acid fragments or variants encoding polypeptides possessing this biological activity. The amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of TGF-β-R are lacking, it is unpredictable as to which encoding fragments and variations, if any, meet the limitations of the claims. Therefore it would require undue experimentation by

one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

9. Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus, i.e polynucleotides encoding polypeptides of limited identity to the disclosed sequences. Applicant has disclosed two species, the isoforms of SEQ ID NOs: 1 and 3, but has not disclosed sufficient species for the broad genus of variants of these polynucleotides.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other TGF-β family members are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative

teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed: there is no guidance in the art as to what the defining characteristics of TGF-β-R might be. Thus, no identifying characteristics or properties of the instant polynucleotides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, the disclosure of SEQ ID NOs:1 and 3 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are additionally rejected because they encompass allelic variants and splice variants. These are molecules that exist in nature and have particular sequences. Unless those sequences are specifically disclosed in the specification, Applicant cannot be said to be in possession of them.

10. Claims 1-8, 10, 11, 43-45, 50, 56, and 57 are further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' referral to the deposit of the plasmids in the specification and in the claims is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his

or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line is required.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-8, 10, 11, 43-45, 56, and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims encompass molecules identified by hybridization under moderately stringent conditions. Applicant has not defined those conditions; only an example is presented on p. 17. Thus the artisan would not know what conditions, and thus what molecules, Applicant intended the claims to encompass.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-8, 10, 11, and 43-45 are rejected under 35 U.S.C. 102(e) as being anticipated by WO200192305-A2, filed 29 May 2001, priority date 31 May 2000.

WO200192305-A2 teaches SEQ ID NO:1, which is 60% identical to instant SEQ ID NO: 1 and has a local similarity of 96.9% (see alignment attached to document). This sequence would bind to the complement of SEQ ID NO:1 under conditions of moderate stringency. Promoters and viral vectors are taught on pp. 32-35 and pharmaceutical compositions are taught on pp. 41 and 42.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 305-3014 or (703) 308-4242.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
June 26, 2003